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THALAMIC AND CORTICAL CORRELATES OF SLEEP SPINDLES IN RATS

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INTRODUCTION

Sleep spindles are among the most prominent oscillations that appear on the encephalogram (EEG) of all mammalian species and humans during non-REM sleep. International Federation of Electroencephalography and Clinical Neurophysiology (IFSECN, 1974) defines sleep spindle as a “group of rhythmic waves characterized by progressively increasing then decreasing amplitude” (1974)¹. It has been demonstrated that sleep spindles are derived from the thalamus due to inhibitory feedback interaction between neurons in the relay thalamic nuclei and reticular thalamic nuclei (RTN). Further, sequences of sleep spindles are distributed over widespread cortical territories. It is known that thalamic sleep spindles co-occur with their cortical equivalents². However, the majority of EEG studies deal with sleep spindles, which appear in the cortex, and little is known about expression of sleep spindles in the thalamus. Our study describes spindle activity at two levels of the thalamo-cortical loop, in the cortex and the thalamus: (in the ventroposteromedial nucleus of thalamus (VPM) and in the RTN).

In the cortex, sleep spindles are topographically discontinuous: two local, anterior and posterior, spindle types are described in Wistar³ and WAG/Rij rats⁴. It is assumed such a topographical divergence of spindle activity originates from the thalamus. Here we estimate the role of a specific part of the thalamus (VPM) and the RTN in the two spindle types by means of cross-spectral analysis. This allowed us to characterize subcortical mechanisms that may govern spatial distribution of sleep spindles over the cortex.

METHODS

Experiments were performed on nine male 11-12 month old WAG/Rij rats (body weight 320-360 g), which were chronically implanted with two epidural electrodes (above the frontal [AP 2; L 2.5] and occipital [AP -7; L 6] areas) and two deep electrodes in the VPM (AP -3.5; L 2.5; H 7.2) and RTN (AP -1.5; L 2.2; H 7.2). Positioning of electrodes was verified with post mortem histological control after staining of brain slices with Nissl staining. The experiments were conducted in accordance with the regulation of animal experimentation in the Netherlands and were approved by the Ethical Committee on Animal Experimentation of Radboud University Nijmegen.

The EEG was recorded in freely moving rats during 5-7 hours in the dark period of the light-dark cycle. EEG signals were band-pass filtered between 1-500 Hz, digitized with 1024 samples/second/per channel and stored on hard disk (Data Acquisition Hardware and Software, DATAQ Instruments, Inc., Akron, OH).

Sleep spindles were visually identified during non-REM sleep using formal criteria^{1,2} and divided on the anterior and posterior types³. 30-70 representatives of each spindle type were collected in each animal. After performing Fast Fourier transformation (FFT), cross-spectrum

was computed in all combinations of four recording channels. Individual cross-spectra were averaged per channel, per spindle type and per animal.

RESULTS AND DISCUSSION

Histological examination showed that in five out of nine rats one deep electrode was successfully implanted in the RTN and in eight of nine rats the other one was positioned in the VPM. EEG data of the rest animals were excluded from analysis. Being recorded in the thalamus, sleep spindles were less well shaped than their cortical equivalents (Fig. 1).

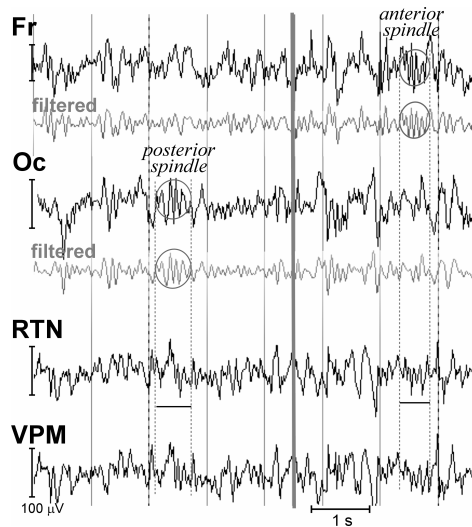


Figure 1. Local cortical sleep spindles as were expressed in the cortex (Fr – frontal and Oc – occipital) and in the thalamus (VPM – the ventroposteromedial thalamic nucleus; RTN – the reticular thalamic nucleus).

During anterior sleep spindles, cross-spectra between two cortical and two thalamic pairs (black lines in Fig. 2A,B) showed two peaks, one around 8-10 Hz and 11-12 Hz for the cortical crossspectrum and 8-9 and 10.5-11.5 for the thalamic crossspectrum. The highest values for the cross spectra were obtained for the ‘frontal cortex – thalamic’ crossspectrum in the 7-14 Hz range, while the values between the occipital cortex and thalamus were very modest, perhaps with a small peak between 6 and 7 Hz (black lines in Fig. 2C).

During posterior sleep spindles (gray lines in Fig. 2), cross spectra of cortical (Fig. 2A) and thalamic (Fig. 2B) pairs contained a peak around 9-10 Hz. The most characteristic cross-spectral pattern was obtained in ‘occipital cortex – VPM’ pair with a moderate peaks at 7 and a second one between 9 and 11 Hz. The cross-spectral association between occipital cortex and RTN were small and centered around 8 Hz. Associations between frontal cortex and the thalamus were very weak (Fig. 2C).

Peak values of cross-spectral curves of the values of individual subjects were averaged (Fig. 3). Anterior sleep spindles expressed in the cortex, the VPM and RTN showed a strong synchrony in the delta range (2.8 Hz), 8.2-8.5 Hz and 10-13 Hz. Posterior sleep spindles showed more a much more simple pattern of cross-spectral associations, which was limited to the mean frequency of the posterior sleep spindles, 10 Hz.

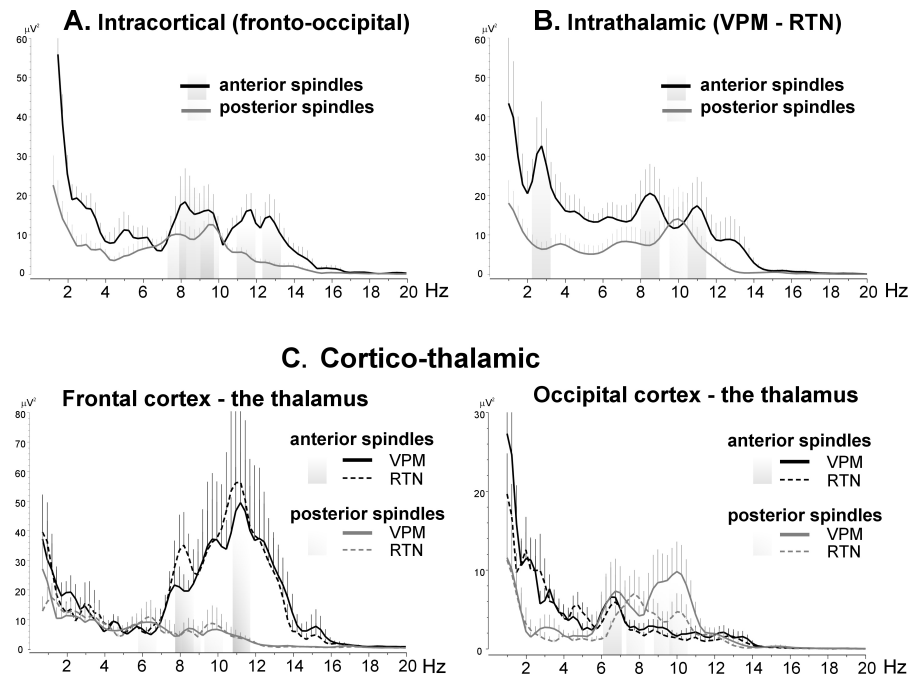


Figure 2. The averaged cross-spectra of six electrode pairs (VPM – ventroposteromedial thalamic nucleus; RTN - reticular thalamic nucleus), mean \pm s.e.m.

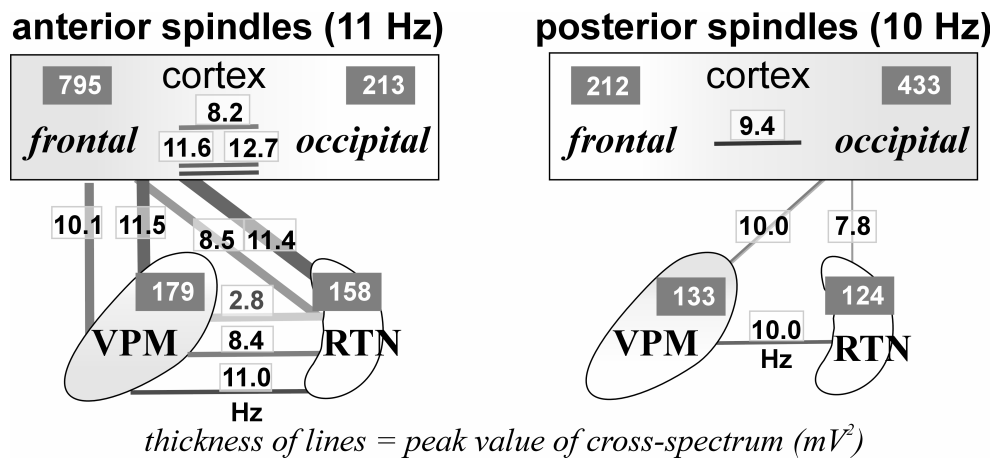


Figure 3. Frequency-specific coupling within thalamo-cortical circuit during anterior and posterior sleep spindles. Peak frequencies are indicated in numbers, Hz; the thickness of connecting lines is proportional to peak amplitude, $\square V^2$. Numbers in gray squares indicate the total power of electrical activity, $\square V^2$.

The presence of 11 and 10 Hz spectral associations between the VPM and RTN suggests that these structures are coupled for the generation of anterior and posterior spindle rhythms. Since the associations between occipital cortex and RTN were restricted to 7.8 Hz and 10 Hz associations were missing, it seems unlikely that the RTN is fully integrated into the

thalamo-cortical loop responsible for generating posterior sleep spindles. Therefore, the role of the RTN in posterior sleep spindles remains doubtful

The frontal cortex, VPM and RTN are anatomically and functionally related and appear to be strongly coupled during anterior sleep spindles.

Direct connections of the occipital cortex with the VPM and the RTN are less evident; this may explain the weak cross-spectral associations during posterior sleep spindles. We hypothesize that the sustaining of posterior sleep spindles involves some other (sub)cortical structures.

More generally, it appears that frontal and occipital cortical areas reveal different functional associations with the thalamus during spindle oscillations. There might be several thalamo-cortical oscillatory networks that produce different sleep oscillations, resulting in topographical distinctions of sleep spindle activity.

CONCLUSIONS

Two topographically distinctive types of sleep spindles, anterior and posterior ones, show different thalamo-cortical network associations.

Anterior sleep spindles strongly involve frontal cortex, specific thalamus (VPM) and RTN, where high associations are found in 2-3, 8-10 and 11-12 Hz. Posterior spindles involve occipital cortex and partly the VPM and RTN, showing limited network associations around 10 Hz. The role of the RTN in posterior sleep spindles remains doubtful: in spite of functional coupling with VPM, the RTN weakly associates with the occipital cortex. Altogether, the source of distinction between two spindle types might lie in the RTN.

ACKNOWLEDGEMENTS

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